Optimal Management of Malignant Polyps, From Endoscopic Assessment and Resection to Decisions About Surgery

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Colorectal cancer is defined clinically as invasion of dysplastic cells into the submucosa. Lesions with submucosal invasion but without invasion into the muscularis propria are generally called malignant polyps.

A stepwise approach produces optimal management of malignant polyps (including polypoid and flat/depressed lesions). The first step is to avoid endoscopic resection of lesions with endoscopic features that predict deep submucosal invasion. Lesions without such features are candidates for endoscopic resection. The second step is to assess candidates for endoscopic resection for features that predict an increased risk of superficial submucosal invasion. Such lesions should be considered for en bloc endoscopic excision if feasible. The third step is giving patients with endoscopically resected malignant polyps good advice regarding whether to undergo adjuvant therapy, usually surgery.

We review the endoscopic and histologic criteria that guide clinicians through these steps.

Keywords:

Malignant polyps; colon polyp; colorectal cancer

Overview of the problem

A malignant colorectal polyp ("malignant polyp" is used generically here and includes polypoid and flat/depressed lesions) can be generally defined as a colorectal lesion with extension of dysplastic elements into the submucosa but not the muscularis propria [1]. In the TMN classification such lesions are pT1 [2]. The general clinical problem posed when an endoscopically resected polyp is reported by a pathologist as malignant is whether to proceed with surgery to resect potential residual cancer in the bowel wall at the site of endoscopic resection, or the lymph nodes outside the bowel wall and near the resection site. However, as described below, optimal endoscopic management involves recognition of endoscopic features of "deep submucosal invasion" which, when present in flat, depressed or sessile lesions, indicates the need to proceed directly to surgical resection without exposing the patient to the risk of endoscopic resection. Furthermore, optimal management includes recognizing lesions that are at higher risk of "superficial submucosal invasion", because *en bloc* resection techniques (if available and feasible) can allow some patients in this group to avoid surgical resection that would be more likely recommended in the case of piecemeal resection.

Decisions regarding management of malignant polyps that are already endoscopically resected can involve input from the endoscopist, one or more pathologists, a general or colorectal surgeon, an oncologist, and should generally involve the patient and/or her family. In some cases of malignant rectal lesions a radiation oncologist may be involved. Involvement of multiple specialists will lead to better informed and improved decisions. However,

endoscopists should have sufficient understanding of malignant polyps to lead the decision making process, and either be the primary professional providing advice to the patient, or be able to contradict unsound advice if another specialist is coordinating care and decision making.

In most centers pathologists do not generally make clinical decisions. However, pathologists play a critical role in the management of resected malignant colorectal polyps. An endoscopist must know what information should be expected from the pathologist, and insist that the pathologic description be complete [1]. Anecdotally, there are many instances where pathologists provide incomplete information, or use terminology that mislead clinicians toward inappropriate decisions and advice to patients [3].

EMR and ESD

Optimal management of malignant polyps involves translating pathology reports of malignant polyps into clinical decisions. Endoscopists must also predict the presence of cancer is deeply invasive and thus should not be resected endoscopically but rather referred directly for surgical resection. Endosocopists should also recognize lesions that have a higher risk of superficial submucosal invasion, as these lesions require a specialized approach to endoscopic resection and specialized handling of the tissue specimen by both the endoscopist and the pathologist. Accurate identification and proper removal of superficially invasive malignant polyps is considered curative (2). In contrast surgical resection may be necessary after piecemeal endoscopic resection and standard handling of resected specimens of a malignant polyp with superficial invasion [3]. The matter of how to resect and handle a lesion that is

suspected to contain superficially invasive cancer leads to an inevitable discussion of the pros and cons of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) [4,5]. The disadvantage of EMR is that in larger flat or sessile lesions it will inevitably be performed piecemeal. ESD however is in its very essence an attempt to resect lesions *en bloc*. Currently in the United States this remains a very challenging situation [4]. Expertise to perform ESD is not widely available, and ESD takes much longer to perform than EMR, is associated with a higher risk of perforation, need for hospitalization, and is without a reimbursement code. Some ESD experts in the U.S. are willing to perform rectal ESD but unwilling to perform colonic ESD, since colonic ESD has a relatively higher risk of complications. A benefit of rectal ESD is that the alternative surgical procedures in the case of malignant rectal polyps are associated with greater morbidity than surgical colonic resections. However, features that predict an increased risk of superficial submucosal invasion in a colorectal polyp, and therefore a candidate lesion for ESD, are as common in the colon as in the rectum. Given the current limited expertise in ESD in the United States, and the other disadvantages of ESD mentioned above, the duty to refer a lesion with an increased (but still low) risk of superficial submucosal invasion must be balanced with the very limited availability and feasibility of ESD in the U.S [4].

Definition of terms

Colorectal cancer is defined by invasion of neoplastic cells through the muscularis mucosa into the submucosa. Without submucosal invasion, the term “cancer” should be

avoided. The lamina propria is the histologic area of the mucosa between the epithelium and the muscularis mucosa. Although some pathologists consider "cancer" in the lamina propria to be "invasive," dysplastic changes in the lamina propria alone does not meet the clinically accepted definition of colorectal cancer [2]. A patient management problem arises when terms such as "intramucosal adenocarcinoma" are used to describe changes in the lamina propria of the mucosa, because any use of the word "adenocarcinoma" can be easily misinterpreted by clinicians and patients as equivalent to cancer, and thereby lead to incorrect decisions [3]. Based on our experience and discussion with Japanese experts, it is more common in the U.S. than in Japan for clinicians to incorrectly believe that colorectal neoplasia confined to the lamina propria and described as " intramucosal adenocarcinoma" has the potential for distant metastasis. Therefore many experts in the U.S. and other western countries recommend that such lesions be termed "high grade dysplasia." Regardless of how they are described by a pathologist, such lesions must be understood by clinicians to have negligible risk of lymphatic or distant spread and are thus considered "benign". That is, all lesions with high grade dysplasia that are completely resected endoscopically have been cured, and do not require salvage surgical treatment.

Unless it has been specifically stated in the pathology report, the endoscopist should contact the pathologist to make sure that any use of the term "adenocarcinoma" in a colon polyp represents submucosal invasion.

"Deep submucosal invasion" refers to submucosal invasion depth greater 1000 microns (equal to 1 mm) and is emerging as an important determinant of prognosis in malignant sessile

and flat lesions. Since deep submucosal invasion predicts a higher risk of residual cancer and angiolymphatic spread and is generally an indication for surgical resection [6]. "Superficial submucosal invasion" refers to submucosal invasion depth less than 1000 microns, and is associated with a much lower risk of residual cancer in bowel wall angiolymphatic spread. These terms are described further below. However, as already suggested, accurate measurement of depth of invasion requires en bloc endoscopic resection, special handling of the resected specimen, and a trained pathologist.

Key clinical decision points

A skilled colonoscopist finds lesions (has a high adenoma detection rate and high detection rate of serrated class lesions), and resects them effectively [7]. Between detection and resection is the critical step of lesion assessment [8]. Every lesion should be assessed according to its size and Paris classification (Figure 1). The surface is also assessed for features that predict deep submucosally invasive cancer (NICE III features – Table 1 or Kudo class V/Vn - Figure 2). Further, adenomatous lateral spreading tumors lesions are classified as granular or nongranular (Figure 3a-f). These data are used to guide a sequence of clinical decisions:

Decision point 1: *Does the lesion have endoscopic features of deep submucosal invasion?* If the lesion has endoscopic features of deep submucosal invasion [9,10], then generally the approach should be to obtain cold biopsy specimens from the portion of the lesion that

demonstrates the features, and the patient should be referred for surgical resection. High quality photographs, ideally with white light and image enhancement [e.g. narrow band imaging (NBI) Olympus Corp. Center Valley, PA, blue light imaging (BLI) Fujifilm Corp, Tokyo, Japan, iScan; Pentax Corp, Montvale, NJ, or dye based chromoendoscopy) should always be taken prior to biopsy. As noted above, deep submucosal invasion refers histologically to > 1,000 microns (1mm) of invasion into the submucosa. This depth of invasion (which requires measurement with an optical micrometer) for accuracy, is associated with a high risk of lymph node metastases [6]. This relationship between the depth of the submucosal tumor invasion and the risk of lymph node metastases was described by Katajima et al [6] and is widely accepted as indicating the need for surgical resection in Japan, although it is infrequently measured by pathologists in the United States. Regardless, the association of certain endoscopic features with deep submucosal invasion can be utilized by endoscopists worldwide. When present, the endoscopic features of deep submucosal invasion are generally ulceration of the lesion surface, and inspection of the ulcerated area demonstrates disruption of the normal vascular and pit pattern [9,10]. These vascular and pit features are embodied in Type III of the NICE classification (Table 1) [10,11] and Type V/Vn of the Kudo classification [9](Figure 2). Surface ulceration and stiffness of the lesion and colon wall are also predictive of deep submucosal invasion, These features (Figure 4a-f) must be understood to be specific for deep submucosal invasion, although they are not sensitive for invasion overall, and are very insensitive for superficial submucosal invasion [12]. Only in instances of a patient who is a very poor surgical candidate should a sessile or flat lesion with endoscopic features of deep submucosal invasion undergo

endoscopic resection. Endoscopists should understand that regardless of the method of endoscopic resection, including ESD, the presence of deep submucosal invasion generally indicates the need of surgical resection. Thus, patients with deep submucosal invasion do not benefit from endoscopic resection including ESD.

The above comments do not necessary apply to a pedunculated lesion that has features of deep submucosal invasion. In a pedunculated lesion a deeper level of submucosal invasion could still be correlated with overall favorable histologic features [6,13-15], and might not warrant subsequent endoscopic resection. Thus*, en bloc* endoscopic snare resection is acceptable in the case of pedunculated adenomas that have features in the polyp head consistent with deep submucosal invasion e.g. (ulceration, NICE III features, Kudo Vn pits, stiffness in the polyp head, unusual thickening of the stalk). Large pedunculated polyps, regardless of whether there are features of deep submucosal invasion in the inspected polyp head, should be resected en bloc. That is, extensive efforts should be made to get the snare entirely over the polyp head and around the stalk only, so that the polyp head will not be resected piecemeal. Moving the snare further down the stalk toward the bowel wall increases the chance that any cancer present will be adequately resected (see below). To correctly assess any cancer that may be present, the pedunculated polyp should be bi-sected through the head and stalk of the polyp by the pathology department [1].

Decision point 2: If the lesion lacks features of deep submucosal invasion, then generally it is a candidate for endoscopic resection, either locally if there is sufficient endoscopic expertise, or at a center with advanced endoscopic expertise. *However, when there is no*

endoscopic evidence of deep submucosal invasion, the endoscopist must now consider if the lesion has a relatively increased risk of superficial submucosal invasion, since a higher risk of superficial submucosal invasion may affect the endoscopic resection approach.

Unfortunately, unlike the case for endoscopic features of deep submucosal invasion, there are no endoscopic predictors of superficial submucosal invasion that have adequate sensitivity or specificity[12]. The endoscopist can only identify predictors associated with a relatively increased risk of superficial invasion, while realizing most lesions with these features will have no submucosal invasion.

From the perspective of endoscopic resection, these issues apply only to nonpedunculated polyps. Pedunculated lesions lacking features of deep submucosal invasion but with substantial size should, like all pedunculated lesions, be resected *en bloc*, and in the case of large size some consideration should be given to moving the snare close to the bowel wall. This positioning increases the length of stalk on the specimen, and increases the possibility of a clear resection margin (see below) in pedunculated malignant polyps.

For lesions with a broad attachment to the colon wall (nonpedunculated), and lacking endoscopic features of deep submucosal invasion, an increased risk of superficial submucosal invasion is associated with nongranular morphology (particularly with depression or bulky sessile shape), with depression in granular lateral spreading tumors (G-LST), and with dominant nodules in G-LSTs [12]. The surface pattern is also helpful at predicting superficial submucosal invasion. Recently, the JNET classification [20](20) expands on the NICE classification to divide the

NICE II lesions (conventional adenomas) into JNET Type II A and Type II B (Table 1), with Type II B having an increased risk of superficial submucosal invasion. However, JNET is designed to be used with magnifying colonoscopes. In the U.S., some degree of optical magnification on colonoscopes is increasingly available, but expertise and experience in using magnification is still very limited. Anecdotally, some Japanese experts believe the near focus (optical magnification) function on the Olympus (Olympus Corp, Center Valley, PA) is adequate to apply the JNET classification, but published evidence to support this suggestion is not yet available.

The endoscopist must understand that the histologic assessment of the depth of submucosal invasion requires an *en bloc* endoscopic resection. That is, superficial submucosal invasion cannot reliably be identified after piecemeal endoscopic mucosal resection. An exception may be when a dominant nodule in a G-LST is resected and submitted separately to the pathologist. Other than this exception piecemeal EMR followed by a pathology reading of any submucosal invasion will lead to a recommendation for surgery regardless of invasion depth.

In addition to an *en bloc* resection, endoscopists should pin the resected specimen on cork board or similar material so it lays flat before adding it to the formalin container. If the specimen is placed directly into formalin without pinning, the edges will curl, rendering the measurement of submucosal invasion depth inaccurate. Assessment of the lateral margins may also be compromised.

For lesions with features associated with an increased risk of superficial submucosal invasion and less than 2 cm in diameter, *en bloc* resection can be achieved by using EMR or ESD.

Lesions > 2 cm usually require ESD to achieve *en bloc* resection. As already noted, most lesions with the endoscopic features noted above that suggest an increased risk of submucosal invasion will have no submucosal invasion, and a few will have deep submucosal invasion. The question arises of how many will have superficial submucosal invasion and therefore benefit from *en bloc* resection by avoiding subsequent surgical resection. In selected Japanese and Korean studies ESD studies in which candidate lesions for ESD were large flat or sessile lesions lacking endoscopic features of deep submucosal invasion, , the answer is about 10% [21-24](21-24). This means that in carefully selected patients with a high risk of superficial submucosal invasion, about 10 ESDs must be performed (number needed to treat or NNT equals 10) for 1 patient to benefit from ESD, and the benefit will be avoiding a subsequent surgery. In some western ESD series, the NNT for one patient to avoid surgery by ESD (because *en bloc* resection of superficial submucosal cancer was achieved) rather than EMR is 30 [25-27](25-27). As noted above, this potential benefit of reduced need for surgery must be weighed against the cost in extra time, risk of perforation, increased need for hospitalization, and lack of reimbursement of ESD compared to piecemeal EMR. Given these considerations, and given that long-term outcomes of piecemeal EMR followed by surgery compared to ESD are comparable, piecemeal EMR of these lesions is within the standard of medical care in the United States. Many clinicians believe the high cost and risks of surgical resection of benign polyps [16-19](16-19), a problem that persists in the United States [28], is quantitatively a much more important healthcare outcomes issue compared to the small number of patients who undergo surgery

after piecemeal EMR of malignant polyps with superficial submucosal invasion compared to following treatment with ESD.

Many of the lesions under consideration are found unexpectedly at the time of a screening/surveillance or diagnostic colonoscopy. In some practice environments clinicians may proceed directly to large EMR. However, many experts now consider large EMR and certainly ESD to be inappropriate without specific consent and expertise. In these settings these lesions should be well-photographed and marked with the smallest volume of tattoo necessary for later endoscopic resection. It is very important to avoid maneuvers that make subsequent EMR or ESD more difficult. These include aggressive tissue sampling (any snare method or even extensive cold biopsy) or tattooing directly under or immediately adjacent to the lesion. Both of these cause submucosal fibrosis which make subsequent EMR/ESD more challenging and riskier. If local expertise for EMR and/or ESD is not available, referral to a regional center with advanced therapeutic endoscopic expertise is needed. These lesions should not be referred directly to surgery regardless of size or morphology, because endoscopic therapy is associated with much lower cost and risk compared to surgery for treatment of benign polyps [16-19](16-19).

Decision point 3: *The polyp has been resected, and the pathology report demonstrates cancer (submucosal invasion). Should the patient undergo surgical resection?* The question

generally implies that the lesion was resected *en bloc*, as noted above. In the case of a pedunculated polyp that has been resected piecemeal, or has not been correctly sectioned in the pathology department so that the both the polyp head and the stalk can be assessed, proper assessment of the malignant features of the polyp may not be possible, and surgical resection may be the best course. In a case of a nonpedunculated polyp resected piecemeal, surgical therapy is generally the preferred course. In the case of *en bloc* resection, the approach to deciding on the need for subsequent surgical resection will vary between pedunculated and nonpedunculated polyps (see below).

Estimating the risk of residual cancer in the bowel wall and lymph nodes after endoscopic resection of malignant *pedunculated* polyps

When submucosal invasion (adenocarcinoma of the colon or rectum is identified in an endoscopically resected polyp, the pathologist must comment on the presence or absent of specific features (Table 2) associated with an increased risk of residual cancer in the bowel wall or lymph nodes. The presence of one or more of these features are generally referred to as the presence of "unfavorable histologic criteria", and would warrant a decision to proceed with surgical resection, unless the risk of surgical resection is considered to outweigh the risk of residual cancer. Poor differentiation [29,30], which is present in about 5-10% of all colorectal cancers, and lymphovascular invasion [31], present in perhaps in 30% of all colorectal cancers, are both considered unfavorable histologic criteria. Unfortunately, both are also subject to

substantial interobserver variation between pathologists[32]. Tumor budding, which refers to separated small (1-3) groups of cancer cells at the lead edge of the cancer [6,33], is less well defined as a poor histologic criterion in pedunculated lesions, but is an unwelcomed feature in any malignant polyp. A criterion that can be considered in every pedunculated polyp is the proximity of the tumor to the resection line. Although the original study by Basil Morson suggested the need for "clear resection margin [34]," a margin of at least 1 mm is advisable [35], and a margin of at least 2 mm is preferred [36,37]. It should be evident that the distance of the tumor from the resection line and the depth of submucosal invasion are two distinct concepts. At least some evidence suggest that the depth of invasion can be greater than 1000 microns in pedunculated polyps, and an excellent prognosis is preserved if all other criteria are favorable [6,13-15]. Another approach to risk evaluation in malignant pedunculated polyps is the Haggett criteria, which essentially state that cancer which is confined to the polyp head (Haggett levels 1,2, 3) is associated with a zero risk of residual cancer while the risk increases with a Haggett level 4 (cancer invading the polyp stalk)[38].

Estimating the risk of residual cancer in the bowel wall and lymph nodes after endoscopic resection of *nonpedunculated* polyps

For nonpedunculated polyps, as noted above for pedunculated polyps, the presence of poor tumor differentiation, lymphovascular invasion, and tumor budding are each considered unfavorable histologic criteria. By definition, cancer in a nonpedunculated polyp is considered

Haggett level 4, and cancer in a nonpedunculated polyp is generally considered to be higher risk for residual disease than cancer in a pedunculated polyp. If resected *en bloc* and appropriately handled by the endoscopist and the pathologist, the depth of invasion can be utilized to separate malignant nonpedunculated polyps with otherwise favorable histologic criteria into low and high risk lesions. One approach to measuring the depth of invasion is to divide the submucosal into 3 levels as described by Kikuchi et al [39]. Cancers confined to the superficial third (SM1) and lacking unfavorable histologic criteria (lymphovascular invasion, poor differentiation, tumor budding) have a low risk of lymph node metastases and metastatic disease, and could be treated conservatively. Because endoscopic resection does not normally include the muscularis propria there is uncertainty as how to divide the submucosa into thirds. Thus the Katajima criterion of greater or less than 1,000 microns of invasion has become standard in Japan [6]. Again, this generally requires *en bloc* resection, proper handling of the specimen with the endoscopist and pathologist, and use of an optical micrometer by the pathologist. This process is seldom carried out in the United States.

Advising the patient after endoscopic resection of a malignant colorectal polyp

When a malignant polyp has been removed by endoscopy, it may be good practice in many instances to obtain a baseline abdominal pelvic and chest CT scan with IV contrast to document absence of metastases, and a baseline CEA level. This should generally be performed at least 3-4 weeks after endoscopic resection to allowed the bowel wall to heal and any

inflammatory lymphadenopathy to resolve. It is critical to understand that these tests have no role in identifying the presence of residual cancer after endoscopic resection of a malignant polyp, and are therefore of no value in assisting the clinician in advising the patient regarding the need for surgical resection. Rather, they serve as a clinical baseline in case there is a need for subsequent evaluation of potentially recurrent disease at a later date. Neither CT scanning, MRI, or endoscopic ultrasound (EUS - in the case of rectal lesions) have sufficient sensitivity to detect residual cancer in the bowel wall or lymph nodes after resection of a malignant polyp [1].

The general process of advising the patient regarding the need for surgery is as follows. For colonic malignant polyps with favorable histologic criteria, the patient is advised that the risk of residual disease is very low but not zero. A healthy patient, particularly if younger, might choose segmental colonic resection and lymph node extraction despite favorable histologic criteria. At the other end of the spectrum, in the case of an elderly patient with multiple comorbidities and unfavorable histologic criteria, observation may be the best course of action. In poor surgical candidates it should be remembered that most patients with unfavorable histologic criteria who undergo surgery will still have a surgical resection that is negative for residual cancer. Cases with borderline histologic criteria and intermediate surgical risk pose the greatest challenge. A widely accepted approach is to discuss the best estimates possible of residual cancer risk and surgical mortality and morbidity with the patient, and encourage them to actively participate in the decision. The estimate of surgical risk may be altered by the surgeon or by a formal risk assessment by another specialist such as a cardiologist or a formal pre-operative risk assessment clinic. The mortality of a segmental colon resection in persons

under the age 50 is below 1%, and is about 3% in healthy 80 year olds [1,16-19,40]. Both age and comorbidities influence the estimate of risk and benefit of surgical resection.

In some cases, where endoscopic resection is deemed to be adequate, it may be appropriate to institute intensive surveillance. In some series, intensive surveillance of malignant polyps without initial surgical resection, by periodic colonoscopy and CT scanning, has identified a substantial rate of cancer recurrences that are still resectable for cure [41].

When surgery is selected, repeat colonoscopy at 1 year, 3 years, and 5 years is warranted for identification of metachronous (and missed synchronous) adenomas and cancer [42].

For malignant rectal lesions, additional considerations apply. A baseline EUS should be performed and consideration can be given to surgical full thickness resection of the endoscopic resection site using a transanal approach. In some centers, EMR or ESD of the ulcer at the resection site is considered to determine if residual neoplasia is present at the resection site. The availability of the endoscopic full thickness resection device for use in the colon [43,44], may increase the use of endoscopic full thickness resection as adjuvant therapy after standard endoscopic resection of malignant polyps in the colon. The morbidity of rectal surgery is higher than colonic surgery, and includes the risk of sexual dysfunction and low anterior syndrome. Further, the risk of local recurrence at any stage is higher for rectal compared to colonic cancers [45]. These factors lead to increased reliance on careful scheduled follow up for early recurrence, and in some cases the use of adjuvant chemoradiation is appropriate, though some centers may require proven residual disease before applying adjuvant chemoradiation.

Conclusions

Optimal management of malignant polyps begins with endoscopic identification of lesions with specific endoscopic predictors of deep submucosal invasion that should be biopsied but not endoscopically resected (unless they are pedunculated). Rather, these lesions should be referred for surgical resection. If features of deep submucosal invasion are absent, the endoscopist should identify features that are associated with a higher risk of superficial submucosal invasion. These features include sessile non-granular lateral spreading lesions, depression in granular and non-granular lateral spreading lesions, and granular lesions with dominant nodules. If feasible en bloc resection of these lesions may allow a patient whose lesion has superficial submucosal invasion to avoid surgery.

Once a malignant polyp has been resected, the endoscopist should be certain that all appropriate information has been provided by the pathologist. Other specialists may provide important perspectives including assessment of surgical risk. The risk-benefit ratio of adjuvant surgical resection or other treatments should be carefully explained to the patient and her family members that she chooses to involve in the decision making process. In the case of a pedunculated malignant polyp, factors that favor surgical resection include piecemeal resection of the polyp head, poor orientation of the polyp head on the histologic slide, poor tumor differentiation, lymphovascular invasion, and proximity of the cancer to the resection line. In the case of a nonpedunculated lesion, surgical resection is favored by piecemeal resection, as well as any findings of poor tumor differentiation, lymphovascular invasion, and tumor budding.

In a non-pedunculated lesion that is resected en bloc and properly assessed histologically, deep (>1000 micron) submucosal invasion favors surgical resection. As the availability and feasibility of endoscopic en bloc resections increases, the importance of proper handling and histologic handling of *en bloc* tissue specimens will increase.

Table 1. The NICE classification

*International NBI Classification (NICE)

	Type 1	**Type 2**	**Type 3**
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels may be present coursing across the lesion	Thick brown vessels surrounding white structures**	Has area(s) with markedly distorted or missing vessels
Surface Pattern	Dark spots surrounded by white	Oval, tubular or branched white structures** surrounded by brown vessels	Distortion or absence of pattern
Most likely pathology	Hyperplastic or sessile polyp (adenoma)	Adenoma**	Deep submucosal invasive cancer

The Japan Narrow Band Imaging Expert Team (JNET)*

	Type 2a	**Type 2b**
Vessel pattern	Regular caliber Regular distribution (meshed/spiral horn)	Variable caliber Irregular distribution

Surface Pattern	Regular (Tubular branched, papillary)	Irregular or obscure
Most likely histology	Low-grade dysplasia	High-grade dysplasia Shallow submucosal invasive cancer

*JNET (The Japan Narrow Band Imaging Expert Team) was developed for magnifying colonoscopes. NICE (Narrow Band Imaging International Colorectal Endoscopic) was developed for high definition non-magnifying colonoscopes. JNET expands on NICE by dividing NICE Type 2 into Types 2a and 2b, associated with low-grade and high-grade dysplasia, respectively.

Table 2. Unfavorable histologic features in malignant pedunculated and non-pedunculated colorectal lesions *

Pedunculated lesions

- Margin between the tumor and cautery line < 2 mm (see text)
- Invasion of the stalk
- Poor differentiation
- Lymphovascular invasion
- Inadequate orientation of the histologic sections

Non-pedunculated lesions

- Piecemeal resection
- Positive resection margins
- Invasion depth > 1000 microns
- Poor differentiation
- Lymphovascular invasion
- Tumor budding
- Inadequate orientation of the histologic sections

Figure legends

Figure 1 The Paris classification of shapes of superficial gastrointestinal neoplasia

Figure 2 The Kudo classification for prediction of histology of colorectal lesions by pit structure analysis

Figure 3. 3a –c . Granular lateral spreading tumors. Note the bumpy surface. 3d-f Nongranular lateral spreading tumors

Figure 4. 4a White light image a non-granular lateral spreading tumor with deep submucosally invasive cancer. The blue circle highlights an area seen in close-up and in magnification in Figure 4b. 4b. Close-up narrow band imaging (NBI) view of the region in the blue circle in 4a. The yellow arrow points to a region of intact vessels of the NICE Type 2 pattern. The red arrow shows an amorphous vascular and surface pattern (NICE Type 3). 4c. White light photograph of a malignant lesion in the cecum. The area within the blue line is seen in close-up and magnification in 4d. 4d Close-up, magnified NBI image of the area within the blue line in 4c. The yellow arrow points to a region of NICE Type 2 (adenomatous) vascular pattern. The red arrows point to areas of disrupted vascular and surface pattern (NICE Type 3) consistent with deep submucosal invasion of cancer. 4e A broad granular lateral spreading tumor in the cecum. The area within the black line is seen in close-up and magnification in 4f. 4f. The yellow arrow points to an area of intact vessels with the NICE Type 2 (adenomatous) pattern. The area within the yellow line is a region of amorphous vascular and surface pattern consistent with deep submucosally invasive cancer (NICE Type 3).

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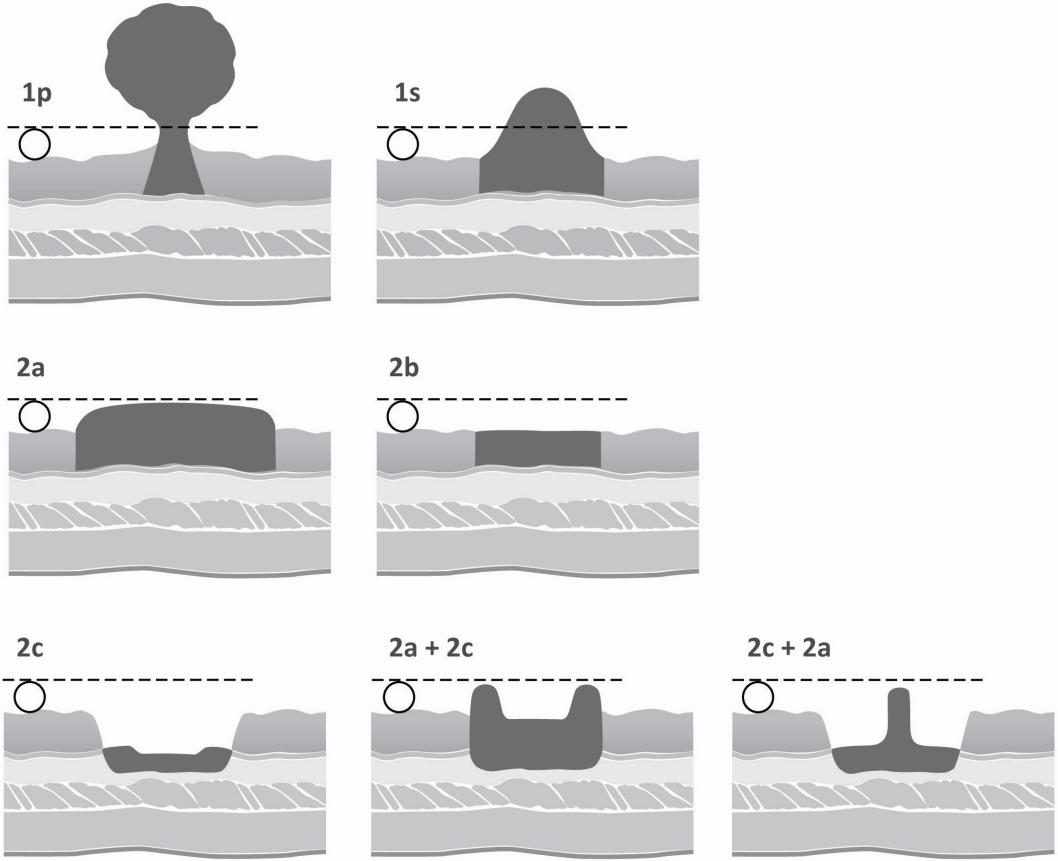
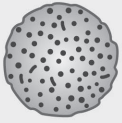

1p
1s
2a
2b
2c
2a + 2c
2c + 2a

TYPE		CHARACTERISTICS	INTERPRETATION
I		Round, normal	Normal
II		Asteroid	Hyperplastic
III_S		Tubular or round pit smaller than normal pit (type I)	Neoplastic Tubular Adenoma
III_L		Tubular or round pit larger than normal pit (type I)	Neoplastic Tubular Adenoma
IV		Dendritic/gyrus brain-like	Neoplastic Tubulovillous or villous
Vi		Irregular arrangement (sizes of III_S, III_L, IV type pits)	Neoplastic High grade or invasive
Vn		Loss or decrease of pits with amorphous structure (non-structural)